

Commentary

Prescribing practices for Betahistine

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Betahistine dihydrochloride (Serc) is an oral preparation of a histamine precursor marketed in Europe as a specific treatment for Meniere's disease. Its proposed mode of action is to cause vasodilation in ischaemic areas of the stria vascularis and dark cells – the areas implicated in the pathogenesis of Meniere's disease. There are a number of flaws in the proposed pharmacological solution to Meniere's disease. One proposed mechanism for the pathophysiology for Meniere's disease is endolymphatic hydrops. However, any drug that increases blood flow to the organs responsible for producing endolymph should theoretically worsen hydrops [1, 2]. Second, it seems to be a contradiction to treat patients with a histamine for a disease that is also relieved by systemic antihistamines [3]. A systematic evaluation of the clinical role of Betahistine for the treatment of Meniere's disease has been undertaken [4]. Only one grade B study and four grade C studies were found, none of which produced convincing evidence for its use.

A definitive diagnosis of Meniere's according to the American Academy of Otolaryngology Head and Neck Surgery guidelines requires audiometrically documented hearing loss on at least one occasion and exclusion of other causes [5]. Such patients would require imaging of the acoustic nerve to exclude an intracranial tumour [6]. Other conditions may mimic the symptoms of Meniere's disease, such as migraine-associated vertigo, and require an alternative treatment strategy [7, 8]. 'Atypical Meniere's disease' encompasses many variants of the classically described triad of symptoms; the underlying pathophysiology, however, is even less well understood. Betahistine has been anecdotally recommended for these entities despite their questionable existence as variants of true Meniere's.

The actual prevalence of Meniere's disease in England is hard to define. Cawthorne and Hewlett have examined the records of eight general practices in England during the year ending March 1952 [9]. The authors were a little vague regarding their methods and the diagnostic criteria used, but their results suggested a prevalence of 157 per 100 000. Goodman in 1956 identified a prevalence of 56

per 100 000 [10] when he closely examined patients passing through a major otology centre in the UK. Other estimates have been proposed, but the methodologies employed have led to ambiguous results. To date the most reliable data we have available regarding the prevalence of Meniere's disease in the UK are from 1956.

The difficulty in calculating the prevalence of Meniere's disease is that official diagnostic criteria are often overlooked and there is a tendency for many physicians to group all cases of recurrent vertigo into the category of Meniere's disease [11]. In the United States Framingham study, when questioned 1.48% of the population claimed to have a history of Meniere's disease [12]. Watanabe *et al.* defined Meniere's as the combination of repeated attacks of true vertigo, fluctuating cochlear symptoms with vertigo, and exclusion of other diseases; the reported prevalence in this Japanese study was 16–17 per 100 000 [13].

Data provided by the Prescription Pricing Authority reveal that 113 000 prescriptions for Betahistine are currently being filled each month in England [14]. The Office for National Statistics reports the population of England to be 50.4 million [15]. Commonly a prescription would be repeated on a monthly basis, and using these figures, the prevalence of Serc usage in England would be 0.2% of the population, or 200 per 100 000. This is clearly higher than the estimated prevalence of Meniere's in 1956 and much higher than studies that have used official diagnostic criteria.

It would be safe to say that a current prevalence of 56 per 100 000 in England would be an overestimate, as there is no evidence of a change in known aetiological factors and it would be more likely that some patients with recurrent vertigo in 1956 would nowadays be given an alternative diagnosis to Meniere's disease due to our improved understanding of other conditions that present with recurrent vertigo. Even using this generous estimation of the current true prevalence of Meniere's disease, only 28 224 people would actually have this condition in England. Prescription cost analysis data are available via a publicly accessible NHS website (<http://www.ic.nhs.uk>). Despite

reservations over the clinical efficacy of Betahistine, restricting its use to only patients with true Meniere's would save over £4 000 000 per annum.

Firm guidelines for the use of Betahistine are hard to find, as even NHS websites provide conflicting advice. Evidence-based organizations, such as the James Lind Alliance, which incorporate the 'Database of Uncertainties about the Effects of Treatments (DUETs)' (<http://www.duets.nhs.uk>), endorse the findings of the above-mentioned Cochrane review. Other NHS websites such as 'Clinical Knowledge Summaries' (<http://www.cks.library.nhs.uk>) sanction the use of Betahistine for prophylaxis, but neither cites any evidence or provides any scientific justification. In the preparation of this article both the National Institute for Health and Clinical Excellence, and the Medicines and Healthcare products Regulatory Agency were contacted regarding national prescribing policy. Neither of these organizations has been involved in the clarification of the therapeutic uses for Betahistine.

Betahistine has few serious side-effects, but there are financial as well as ethical implications in prescribing a sometimes lifelong drug regime in the absence of a definitive diagnosis. Patients with symptoms of Meniere's disease are often challenging to manage, a variety of medical as well as surgical treatments may be available to them, and other more serious pathology may need to be considered. The authors recommend that patients with symptoms of Meniere's disease are appropriately managed by an Otolaryngologist with an interest in Meniere's disease and the initiation of a potentially life long treatment with Betahistine is given careful consideration. Despite a confident diagnosis of Meniere's disease, a pharmacological treatment remains elusive, particularly because the underlying pathophysiology of this condition remains to be proven. More basic science work is required to formulate an evidence-based treatment for Meniere's disease, and any further guidance should be disseminated from high-quality trials led by basic scientists.

REFERENCES

- 1 Blair RL. Medical management of vestibular dysfunction. *Otolaryngol Clin North Am* 1984; 17: 679–84.
- 2 Ruckenstein MJ, Rutka JA, Hawke M. The treatment of Meniere's disease: Torok revisited. *Laryngoscope* 1991; 101: 211–8.
- 3 Moffat DA, Ballagh RH. Meniere's disease. In: Scott-Brown's *Otolaryngology*, 6th edn, Vol. 3, Chapter 19, ed Booth JB. Oxford: Butterworth-Heinemann, 1997: 1–50.
- 4 James AL, Burton MJ. Betahistine for Meniere's disease or syndrome. *Cochrane Database Syst Rev* 2001; (1): CD001873.

- 5 American Academy of Otolaryngology-Head and Neck Foundation, Inc. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease. *Otolaryngol Head Neck Surg* 1995; 113: 181–5.
- 6 Morrison GA, Sterkers JM. Unusual presentations of acoustic tumours. *Clin Otolaryngol Allied Sci* 1996; 21: 80–3.
- 7 Minor LB. Meniere's disease and migraine. *Arch Otolaryngol Head Neck Surg* 2005; 131: 460.
- 8 Parker W. Meniere's disease. Etiologic considerations. *Arch Otolaryngol Head Neck Surg* 1995; 121: 377–82.
- 9 Cawthorne T, Hewlett A. Meniere's disease. *Proc R Soc Med* 1954; 47: 663–70.
- 10 Goodman WS. Aural vertigo: its diagnosis and treatment – a survey of 268 cases. *J Laryngol Otol* 1957; 71: 339–55.
- 11 Slater R. Vertigo. How serious are recurrent and single attacks? *Postgrad Med* 1988; 54: 58–67.
- 12 Mosicki EK, Elkins EF, Baum HM, McNamara PM. Hearing loss in the elderly: an epidemiologic study of the Framingham Heart Study Cohort. *Ear Hear* 1985; 6: 184–90.
- 13 Watanabe Y, Mizokoshi K, Shojaku H, Watanabi I, Hinoki M, Kitahara M. Epidemiological and clinical characteristics of Menieres disease in Japan. *Acta Otolaryngol Suppl* 1995; 519: 206–10.
- 14 NHS Business Services Authority. Prescription Pricing Division. 2007. Available at <http://www.ppa.org.uk> (last accessed 4 December 2007).
- 15 Office for National Statistics. 2005 Mid-year Population Estimates: Office for National Statistics, General Register Office for Scotland and Northern Ireland Statistics and Research Agency.

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